# Antidiabetic Drugs in Patients with Chronic Kidney Disease

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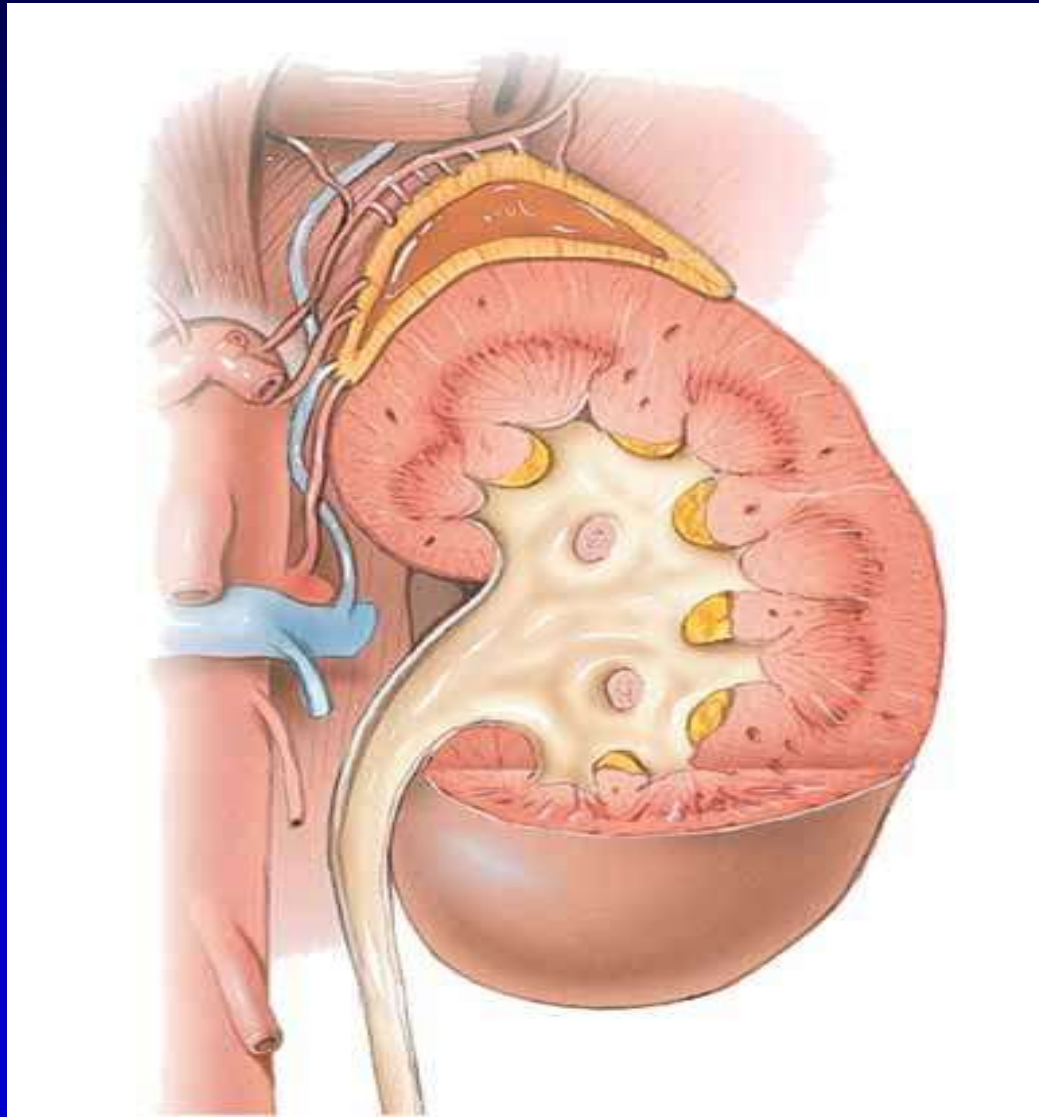
Delta
Diabetes
Association


Education
Shift

# Role of the kidney in glucose homeostasis

- Contributes up to 20% of gluconeogenesis (more post-prandially).
- Accounts for about 10% of total body glucose utilisation.
- Filters and reabsorbs up to 180g of glucose per day.



# CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO

- CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health and CKD is classified based on cause, GFR category, and albuminuria category (CGA).

## Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

| GFR categories (ml/min/1.73 m²) Description and range | | | Persistent albuminuria categories Description and range | | |
|---|---|---|---|---|---|
| | | | A1 | A2 | A3 |
| | | | Normal to mildly increased | Moderately increased | Severely increased |
| | | | <30 mg/g <3 mg/mmol | 30-[illegible] mg/g 3-[illegible] mmol | >300 mg/g >30 mg/mmol |
| G1 | Normal or high | ≥90 | | | |
| G2 | Mildly decreased | 60-89 | | | |
| G3a | Mildly to moderately decreased | 45-59 | | | |
| G3b | Moderately to severely decreased | 30-44 | | | |
| G4 | Severely decreased | 15-29 | | | |
| G5 | Kidney failure | <15 | | | |

Previously micro-albuminuria

Previously macro-albuminuria

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3:136-150.
http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf Accessed February 26, 2013

# ADA 2014: Definitions of Abnormalities in Albumin Excretion

| Category | Spot collection (µg/mg creatinine) |
|---|---|
| Normal | <30 |
| Increased urinary albumin excretion* | ≥30 |

*Historically, ratios between 30 and 299 have been called microalbuminuria and those 300 or greater have been called macroalbuminuria (or clinical albuminuria).



ADA. VI. Prevention, Management of Complications. Diabetes Care 2014;37(suppl 1):S44; Table 11

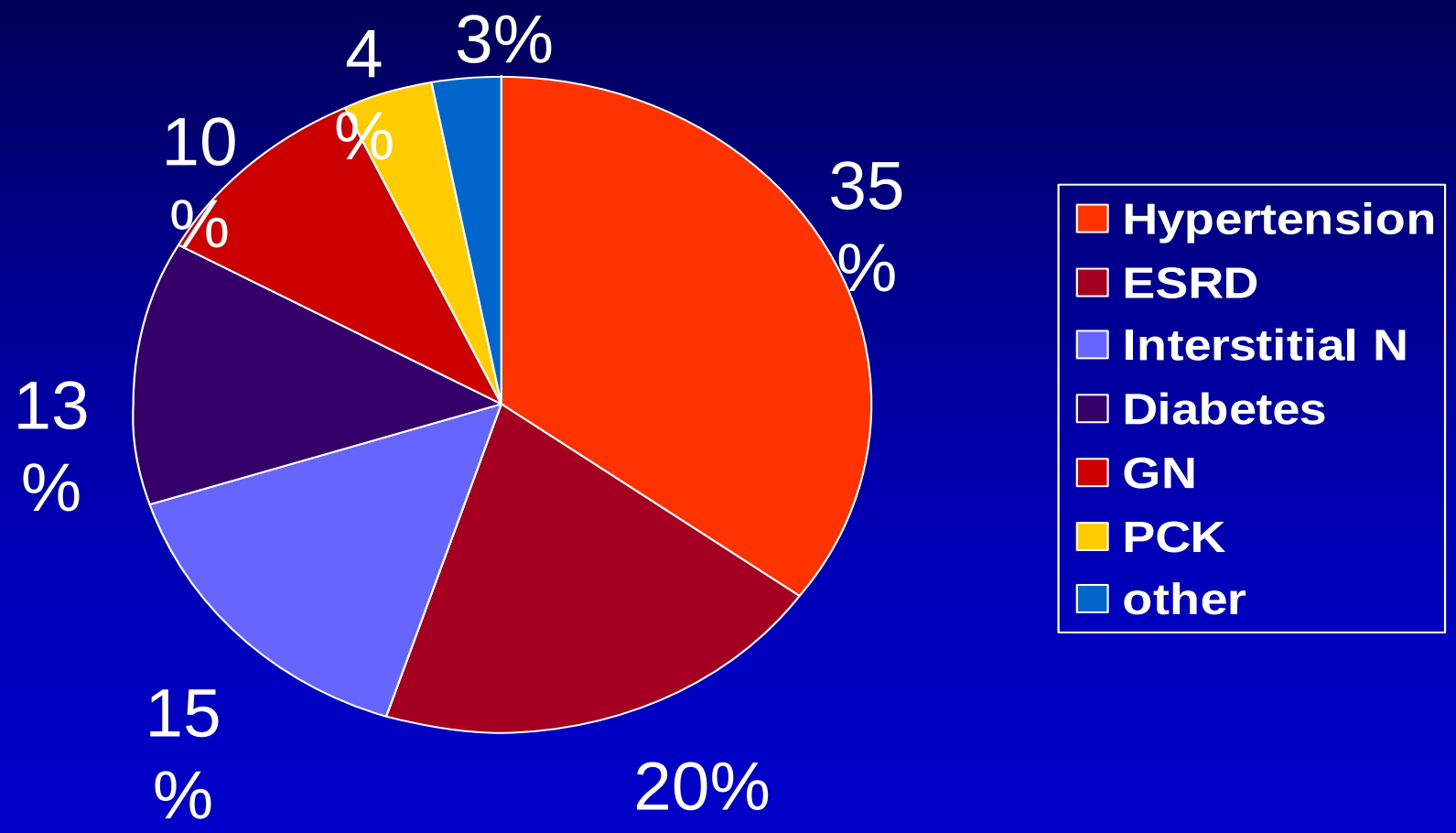
# Factors affecting urinary albumin excretion

| Increases AER | Decreases AER |
| --- | --- |
| ▪ Strenuous exercise<br>▪ Poorly controlled DM<br>▪ Heart failure<br>▪ UTI<br>▪ Acute febrile illness<br>▪ Uncontrolled HPT<br>▪ Haematuria<br>▪ Menstruation<br>▪ Pregnancy | ▪ NSAIDs<br>▪ **ACE inhibitors** |

# AGENDA:

- Magnitude of the problem.
- CKD and CVD.
- The facts in diabetes and CKD.
- Diabetic nephropathy.
- HBA1c Targting.
- Glucose monitoring.
- Management of Dyslipidemia & HTN in DKD.
- Modifications of antidiabetic drugs in DKD.
- Conclusions

# Aetiology of CKD in Egypt




Barsoum RS, Kidney International Supplements (2013) 3, 164–166


The rates of diabetes in Egypt has significantly increased exceeding international rates, (IDF ,2016).

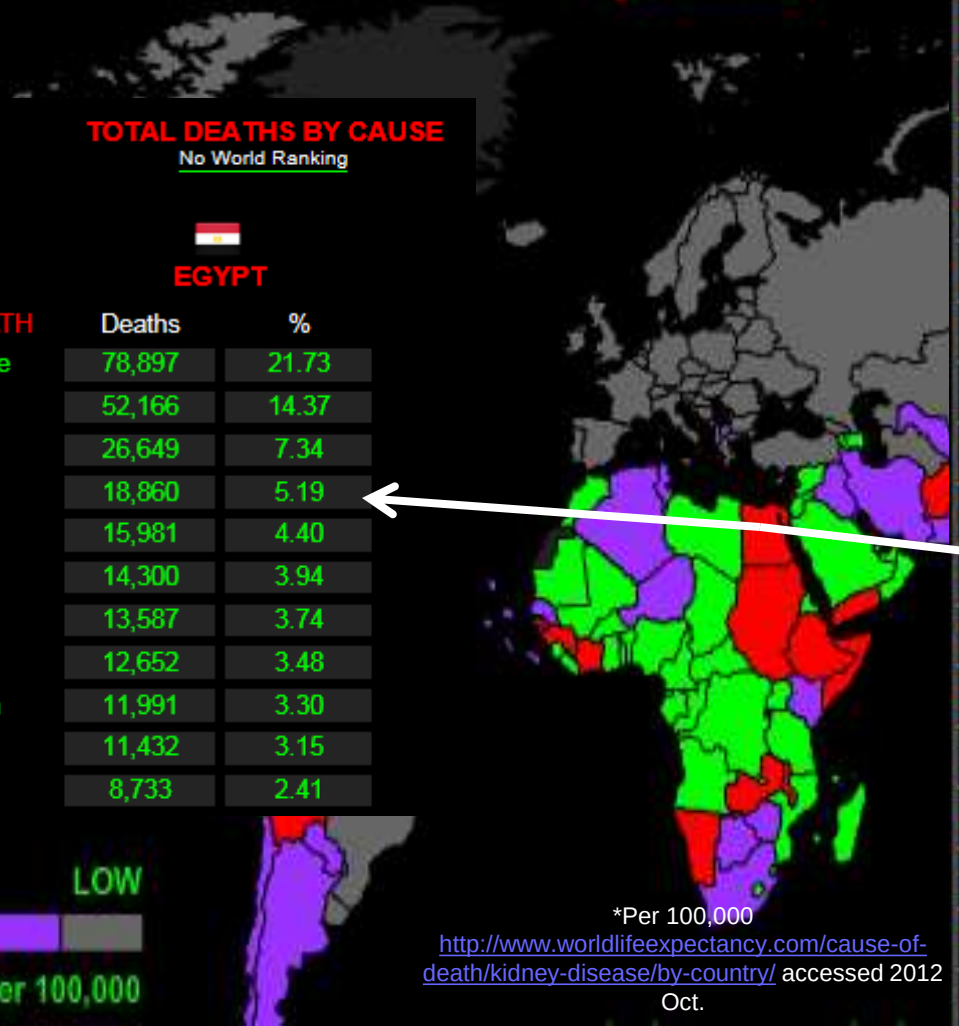
Egypt is now ranked eighth highest in the world in terms of the disease.

# Rate of Kidney Diseases in Egypt is 36.4* with About 5.19% Deaths

RETURN WORLD HEALTH MENU

## KIDNEY DISEASE

Death Rate Per 100,000
Age Standardized



### TOTAL DEATHS BY CAUSE

No World Ranking

EGYPT

| TOP 50 CAUSES OF DEATH | Deaths | % |
|---|---|---|
| 1 Coronary Heart Disease | 78,897 | 21.73 |
| 2 Stroke | 52,166 | 14.37 |
| 3 Liver Disease | 26,649 | 7.34 |
| 4 Kidney Disease | 18,860 | 5.19 |
| 5 Road Traffic Accidents | 15,981 | 4.40 |
| 6 Hypertension | 14,300 | 3.94 |
| 7 Low Birth Weight | 13,587 | 3.74 |
| 8 Endocrine Disorders | 12,652 | 3.48 |
| 9 Influenza & Pneumonia | 11,991 | 3.30 |
| 10 Diabetes Mellitus | 11,432 | 3.15 |
| 11 Congenital Anomalies | 8,733 | 2.41 |

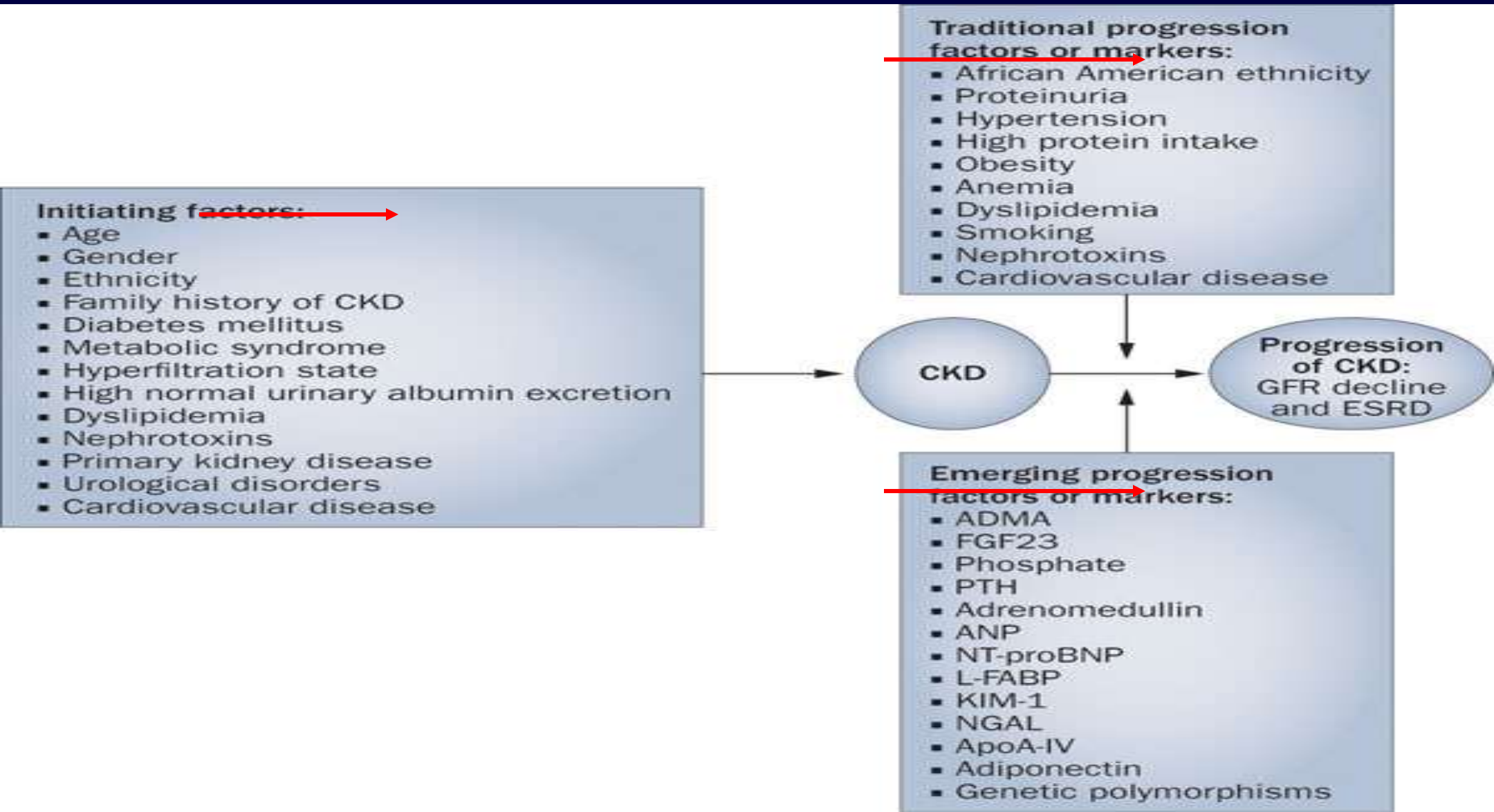
HIGH LOW

Death Rate Per 100,000

| Rank | | Country | Rate | Rank | |
|---|---|---|---|---|---|
| 1 | | EL SALVADOR | 61.2 | 65 | |
| 2 | | MARSHALL ISL. | 60.6 | 66 | |
| 3 | | AFGHANISTAN | 53.3 | 67 | |
| 4 | | NAURU | 53.2 | 68 | |
| 5 | | BOLIVIA | 45.7 | 69 | |
| 6 | | TUVALU | 45.6 | 70 | |
| 7 | | SOMALIA | 44.4 | 71 | |
| 8 | | HONDURAS | 42.6 | 72 | |
| 9 | | SUDAN | 42.4 | 73 | |
| 10 | | NICARAGUA | 41.3 | 74 | |
| 11 | | DJIBOUTI | 36.4 | 75 | |
| 12 | | EGYPT | 36.4 | 76 | |
| 13 | | THAILAND | 36.2 | 77 | |
| 14 | | BAHRAIN | 36.2 | 78 | |
| 15 | | MALAWI | 35.8 | 79 | |
| 16 | | FIJI | 34.4 | 80 | |
| 17 | | YEMEN | 34.1 | 81 | |
| 18 | | COTE D IVOIRE | 31.8 | 82 | |

*Per 100,000
http://www.worldlifeexpectancy.com/cause-of-death/kidney-disease/by-country/ accessed 2012 Oct.

# Factors involved in the initiation and progression of CKD

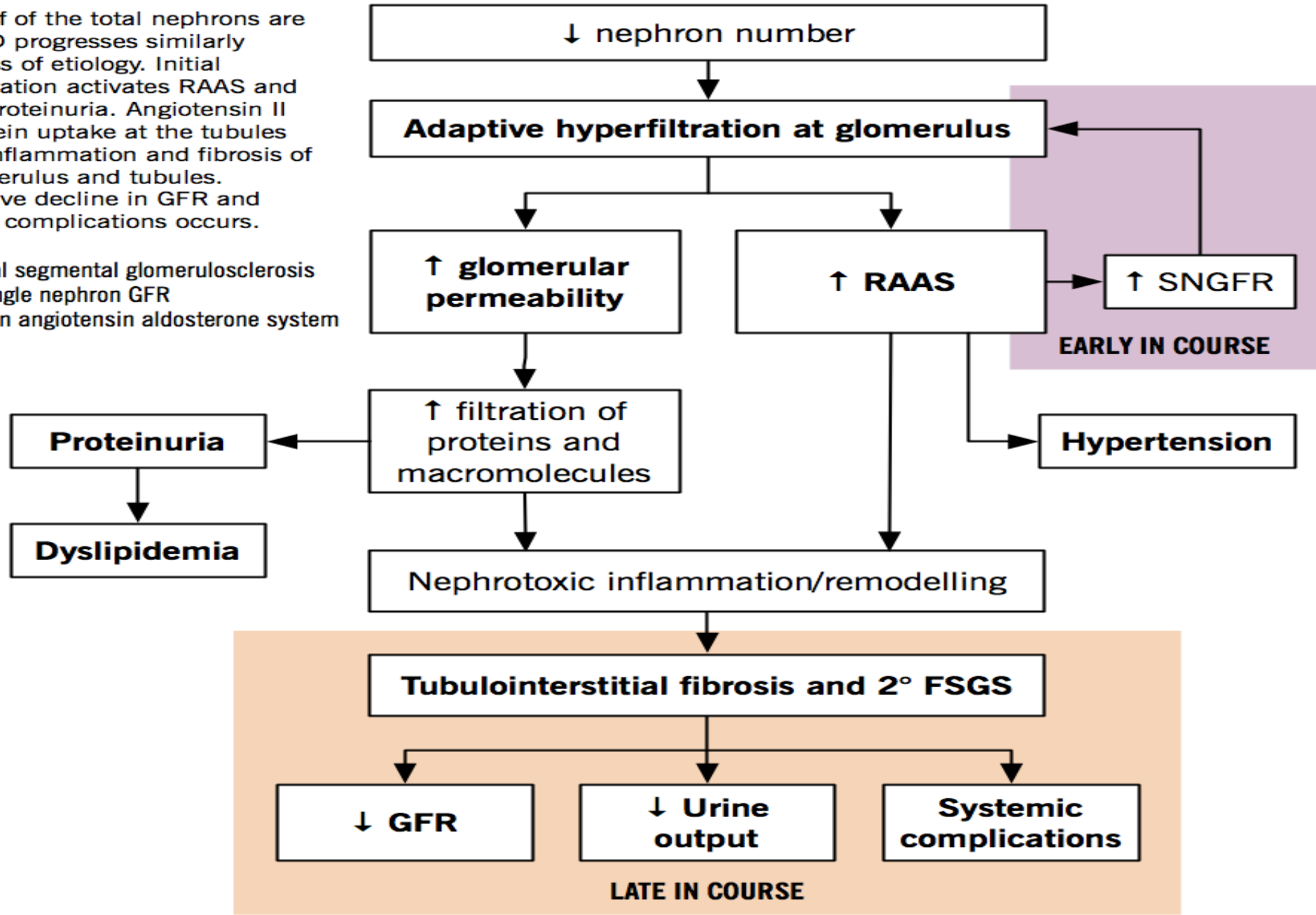


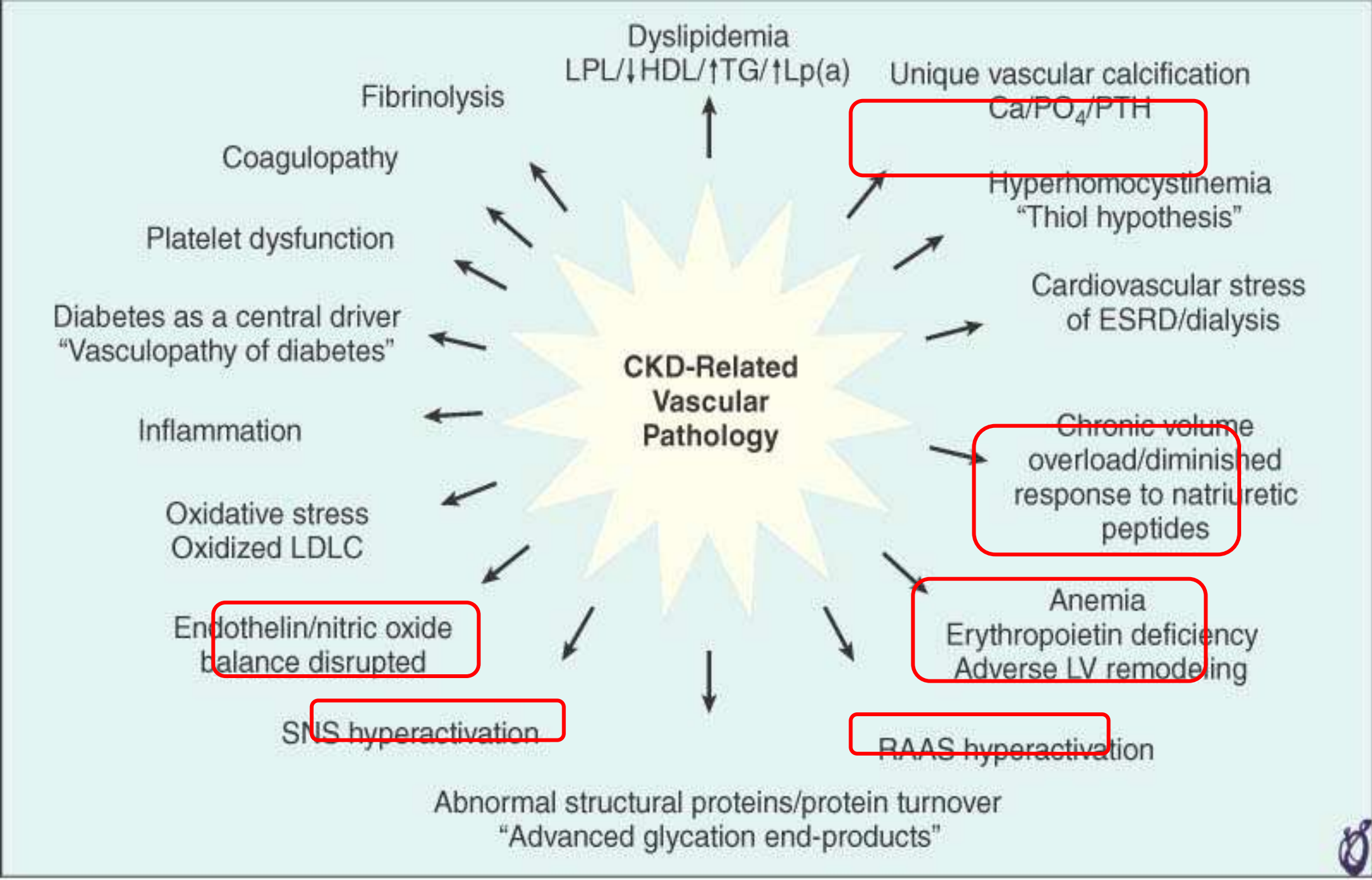
# Pathogenesis of chronic kidney disease

Eric Wong

Once half of the total nephrons are lost, CKD progresses similarly regardless of etiology. Initial hyperfiltration activates RAAS and causes proteinuria. Angiotensin II and protein uptake at the tubules causes inflammation and fibrosis of the glomerulus and tubules. Progressive decline in GFR and systemic complications occurs.

**FSGS** Focal segmental glomerulosclerosis
**SNGFR** Single nephron GFR
**RAAS** Renin angiotensin aldosterone system






*(Modified from McCullough PA: Why is chronic kidney disease the "spoiler" for cardiovascular outcomes? J Am Coll Cardiol 41;725, 2003.)*


CKD
CVD
Kidney Failure
Heart Failure
End-Stage
Decreased GFR
Progression
CVD Events
Albuminuria
Initiation
CAD, LVH
At Increased Risk
DIABETES
HTN, Age, Family History


Fix the Defect

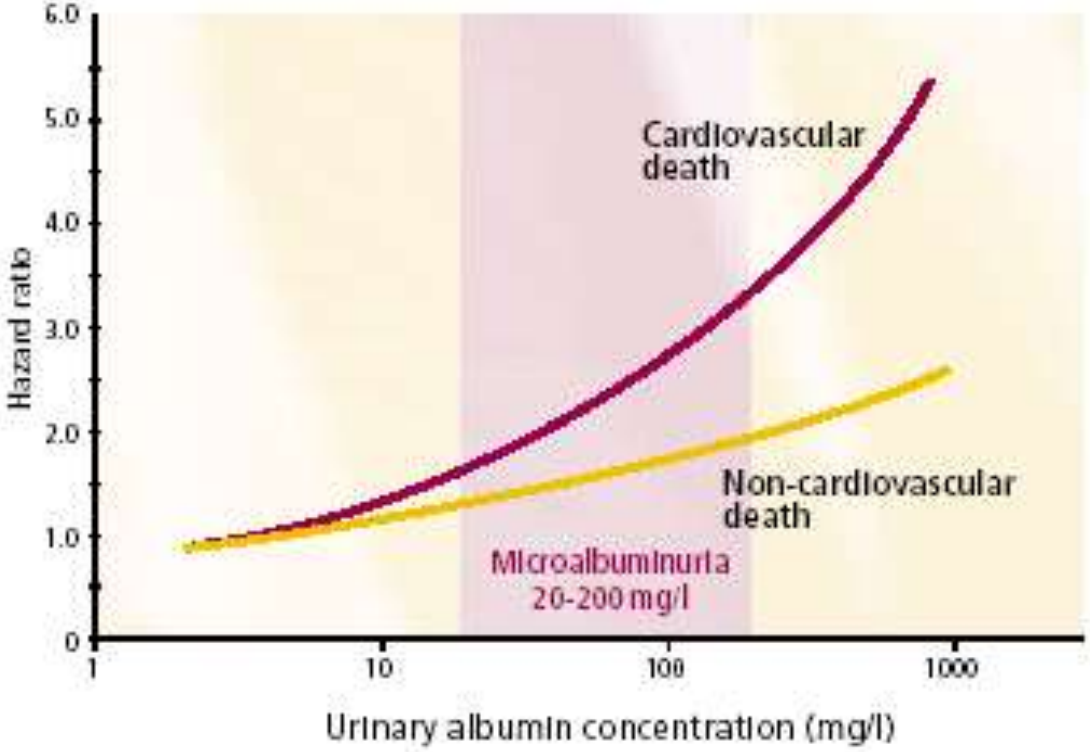
# The facts in Diabetics

- Almost one in three people with type 2 diabetes develops overt kidney disease.
- Diabetes is the single most common cause of end stage renal failure.
- Kidney disease accounts for 21 per cent of deaths in type 1 and 11 per cent of deaths in type 2.

# So How Big Is The Risk In Diabetes?

# Diabetic Nephropathy:

- **Diabetic nephropathy** develops in **30–40%** of patients with type 2 diabetes and constitutes a serious late complication.[3]

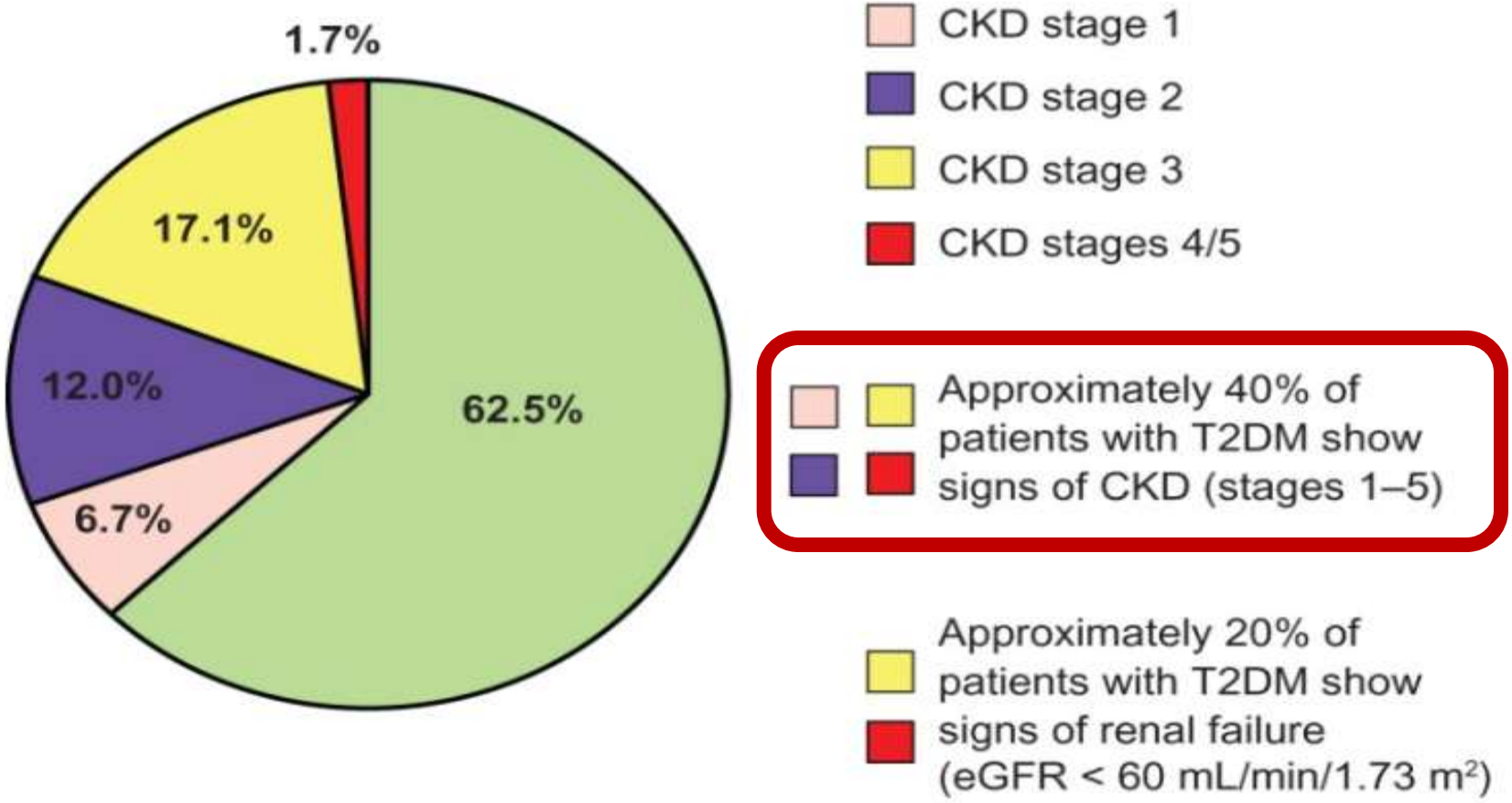



**Effect of urinary albumin excretion on hazard ratio**

Estimated relation when logarithmic hazard is modeled as linear function of urinary albumin concentration.[5]

- **Microalbuminuria** is a strong and independent determinant of **coronary heart disease and death.**[4]

# Renal Dysfunction Is Common in Patients with Type 2 Diabetes




Russo E, et al. Diabetes Metab Syndr Obes. 2013; 6: 161–170.

# What are Diabetics with Nephropathy Dying From?

Stroke

Myocardial Infarction

Heart Failure

Sudden Death

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Facing the
Problem..

# Recommended Goals for Management of Hyperglycemia in Diabetics with DKD

**~7.0%**

to prevent or delay progression of the microvascular complications of diabetes, including DKD

**Not <7.0%**

in patients at risk of hypoglycemia.

**>7.0%**

In individuals with co-morbidities or limited life expectancy and risk of hypoglycemia

## HbA1c Target

National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. *Am J Kidney Dis*. 2012;60(5):850-886.

National Kidney Foundation® KDOQI

# Glucose monitoring in patients with DKD

- A1c
- Fructosamine
- Glycated Albumin (GA)
- CGM
- SMBG

# Nutrition Recommendations in patients with DKD

**Table 5—Macronutrient recommendations in DKD**

| Organization | Lower ranges of dietary protein intake | Higher ranges of dietary protein intake | Carbohydrate | Fatty acids | Sodium |
|---|---|---|---|---|---|
| KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (22) | 0.8 g protein/kg/day in adults with diabetes and GFR <30 mL/min/1.73 $m^2$ with appropriate education | Avoid protein intake >1.3 g/kg/day in adults with CKD at risk for progression; specific comment for DKD not provided | Specific recommendation not provided | Specific recommendation not provided | Lower salt intake to <2 g of sodium per day (5 g of sodium chloride), unless contraindicated |
| KDOQI 2007 Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease (4) | Recommended dietary allowance of 0.8 g/kg body weight per day for people with DKD and CKD stages 1–4 | Avoid high-protein diets defined as ≥20% of total daily calories | Specific recommendation not provided | Increase intake of omega-3 and omega-9 fatty acids | Reduction of intake 2.3 g/day as recommended by the DASH diet |

# Dyslipidemia Management Recommendations in patients with DKD

- No statin therapy for diabetic patients on dialysis.
- Patients receiving statins before dialysis may continue therapy.
- Drug dosing should consider severity of kidney disease.
- No dosage adjustments for niacin, ezetimibe, atorvastatin, or pravastatin.
- Reduce dose of fibrates, fluvastatin, lovastatin, rosuvastatin, and simvastatin in patients with stage 4/5
- Improved outcomes with statin is based primarily on prevention of CVD with no evidence of improved kidney disease outcomes.

**Table 7.** Dose Adjustment for Lipid Lowering Medicines in CKD

| Medication Class and Agents | No CKD or stages 1-2 | CKD stage 3 | CKD stages 4-5 | Kidney transplant |
|---|---|---|---|---|
| **Statins (mg/day)** | | | | |
| Atorvastatin | 10-80 | 10-80 | 10-80 | 10-20 |
| Fluvastatin | 20-80 | 20-80 | 10-80 | 10-80 |
| Lovastatin | 10-80 | 10-80 | 10-40 | 10-40 |
| Pravastatin | 10-40 | 10-40 | 10-20 | 10-20 |
| Rosuvastatin | 5-40 | 5-20 | 5-10 | 5 |
| Simvastatin | 5-40 | 5-40 | 5-20 | 5-20 |
| **Bile acid sequestrants (g/day)** | | | | |
| Cholestipol | 5-30 | 5-30 | 5-30 | 5-30 |
| Cholestyramine | 4-16 | 4-16 | 4-16 | 4-16 |
| Colesevelam | 2.6-3.8 | 2.6-3.8 | 2.6-3.8 | 2.6-3.8 |
| **Fibric acid derivatives (mg/day)** | | | | |
| Bezafibrate* | 400-600 | 200 | Avoid | Avoid |
| Clofibrate | 1000-2000 | 500 | 500 | Avoid |
| Ciprofibrate* | 200 | Unknown | Avoid | Unknown |
| Fenofibrate | 96 | 48 | Avoid | Avoid |
| Gemfibrozil | 1200 | 1200 | 600 | 600 |
| **Other (mg/day)** | | | | |
| Ezetimibe | 10 | 10 | 10 | Unknown |
| Niacin | 2000 | 2000 | 1000 | Unknown |

*Not currently licensed for use in the U.S.

# Hypertension

- ACE I  and ARBs are standard in management of HTN in diabetics with DKD.
- RAS blockade suppress the RAS but  serum aldosterone remains elevated.
- Elevated aldosterone may contribute to the progression of CKD.
- RAS blockade is associated with a reduction of proteinuria and slower progression of kidney disease.
- Close monitoring for  hyperkalemia is mandatory.
- For patients with an e-GFR < 30 ml/min/1.73 m2, thiazide diuretics should be replaced with loop diuretics.

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Communications

ADA 2015 Guidelines

# Management of High Blood Pressure

| | |
|---|---|
| Screening | Measure BP at every visit; confirm elevated BP at separate visit |
| Treatment targets | Diabetes and hypertension: SBP <140 mm Hg<br>• Lower SBP targets (eg, <130 mm Hg) may be appropriate*<br>Diabetes: DBP <90 mm Hg<br>• Lower DBP target (eg, 80 mm Hg) may be appropriate* |
| Treatment | BP >120/80 mm Hg: lifestyle changes<br>• Weight loss (if overweight) • DASH-style diet incl sodium restriction, potassium increase • Moderate alcohol intake • Increased physical activity |
| | BP >140/90 mm Hg: lifestyle changes + pharmacologic therapy<br>• Diabetes and hypertension: ACEI or ARB†<br>• ≥2 agents, incl thiazide-type diuretic, ACEI, or ARB, at max doses usually required to achieve targets<br>• Administer ≥1 agent at bedtime<br>• ACEI, ARB, diuretic: monitor serum creatinine/eGFR and serum potassium |
| Treatment and targets for pregnant women | Diabetes and hypertension: 110-129/65-79 mm Hg target<br>ACEI, ARB contraindicated |

*In certain individuals (eg, younger), if achieved without treatment burden; †If one class not tolerated, substitute another class
ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; DASH=Dietary Approaches to Stop Hypertension; DBP=diastolic blood pressure; eGFR=estimated glomerular filtration rate; SBP=systolic blood pressure

American Diabetes Association. *Diabetes Care*. 2015;38(suppl 1):S1-S93.

# Diabetes mellitus

| Recommendations | Class | Level |
|---|---|---|
| While initiation of antihypertensive drug treatment in diabetic patients whose SBP is ≥160 mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is ≥140 mmHg. | I | A |
| A SBP goal <140 mmHg is recommended in patients with diabetes. | I | A |
| The DBP target in patients with diabetes is recommended to be <85 mmHg. | I | A |
| All classes of antihypertensive agents are recommended and can be used in patients with diabetes; blockers of the renin-angiotensin system may be preferred, especially in the presence of proteinuria or microalbuminuria. | I | A |
| It is recommended that individual drug choice takes comorbidities into account. | I | C |
| Simultaneous administration of two blockers of the renin-angiotensin system is not recommended and should be avoided in patients with diabetes. | III | B |

www.escardio.org/guidelines

Eur Heart J, 2013; 34: 2159-2219
J Hypertens, 2013; 31: 1281-1357
Blood Pressure, 2013: 193-278

ESH European Society of Hypertension

EUROPEAN SOCIETY OF CARDIOLOGY®

# Nephropathy

| Recommendations | Class | Level |
|---|---|---|
| Lowering SBP to <140 mmHg should be considered. | IIa | B |
| When overt proteinuria is present, SBP values <130 mmHg may be considered, provided that changes in eGFR are monitored. | IIb | B |
| Blockers of the renin-angiotensin system are more effective in reducing albuminuria than other antihypertensive agents, and are indicated in hypertensive patients in the presence of microalbuminuria or overt proteinuria. | I | A |
| Reaching BP goals usually requires combination therapy, and it is recommended to combine blockers of the renin-angiotensin system with other antihypertensive agents. | I | A |
| Combination of two blockers of the renin-angiotensin system, though potentially more effective in reducing proteinuria, is not recommended. | III | A |
| Aldosterone antagonists cannot be recommended in CKD, especially in combination with a blocker of the renin-angiotensin system, because of the risk of excessive reduction in renal function and of hyperkalaemia. | III | C |

www.escardio.org/guidelines

Eur Heart J, 2013; 34: 2159-2219
J Hypertens, 2013; 31: 1281-1357
Blood Pressure, 2013: 193-278

ESH European Society of Hypertension

EUROPEAN SOCIETY OF CARDIOLOGY®

# Diabetes Drugs Modification with DKD

- Metformin.
- SU.
- Glinides.
- AGI’s.
- TZD’s.
- Insulins.
- Amylin agonists.
- SGLT2-Inhibitors.
- GLP1-RA.
- DPP4-inhibitors.

# Time To ...
# Think Before Use Anti-Diabetic Drugs

Kindly think

# Renal impairment is a well recognized predisposing factor to hypoglycemia

**40-50% of insulin is metabolized by the kidney**

**Accumulation of hypoglycemic agents**

**Small part of gluconeogenesis occurs in the kidney**

Russo E, et al. Diabetes Metab Syndr Obes. 2013; 6: 161–170.
http://www.medscape.org/viewarticle/437273
http://www.elmhurst.edu/~chm/vchembook/604glycogenesis.html

# Solving the Challenges….achieving the balance

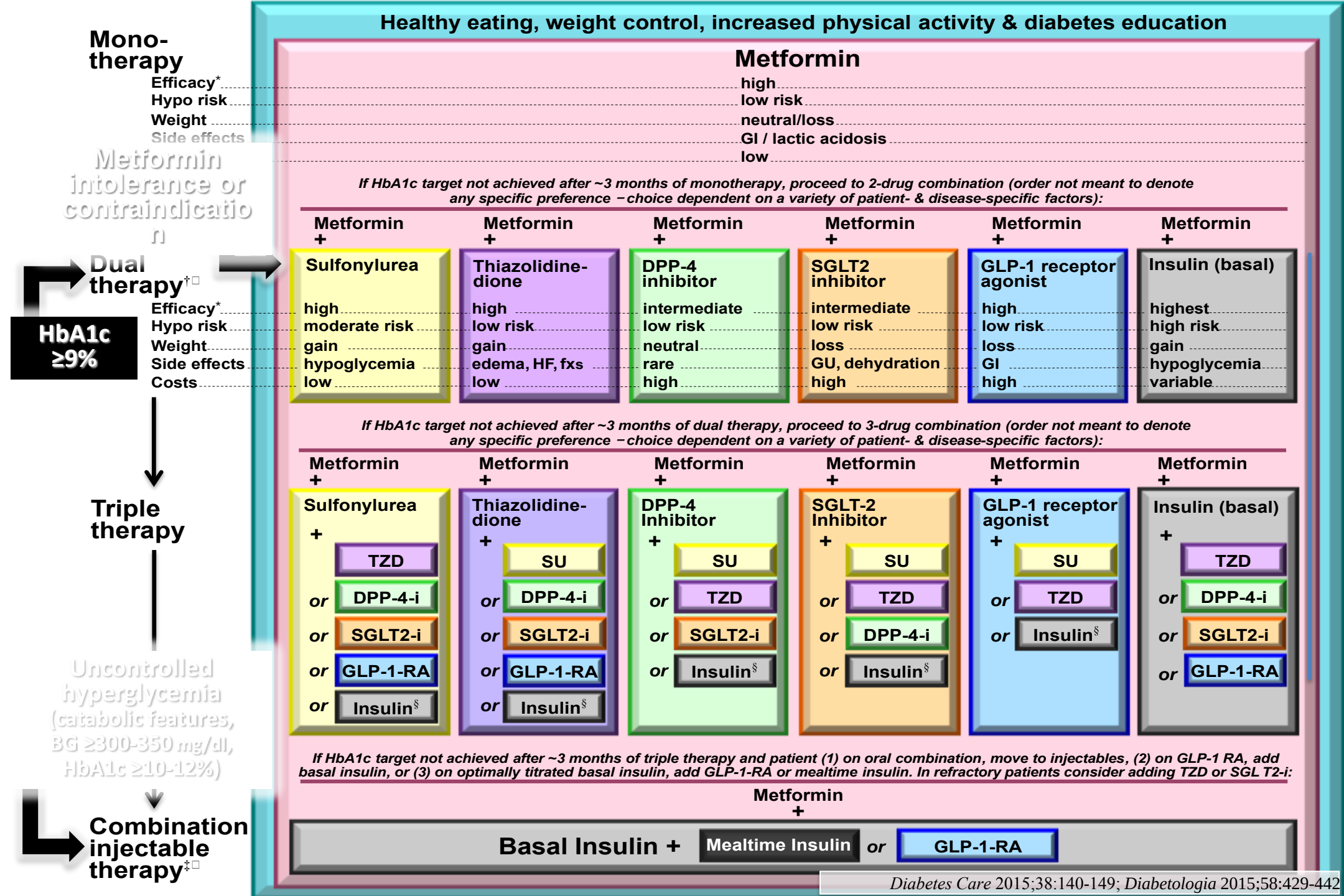
# When start, start right


# ADA-EASD Position Statement Update: Management of Hyperglycemia in T2DM, 2015

## ANTI-HYPERGLYCEMIC THERAPY

- **Glycemic targets**

- **HbA1c < 7.0%** (mean PG ~150-160 mg/dl [8.3-8.9 mmol/l])
- Pre-prandial PG <130 mg/dl (7.2 mmol/l)
- Post-prandial PG <180 mg/dl (10.0 mmol/l)
- ***Individualization*** is key:
  - Tighter targets (6.0 - 6.5%) - younger, healthier
  - Looser targets (7.5 - 8.0%$^{+}$) - older, comorbidities, hypoglycemia prone, etc.
- Avoidance of hypoglycemia




*Diabetes Care* 2015;38:140-149; *Diabetologia* 2015;58:429-442

# WHAT TO DO!

# Modifications in Diabetes drugs with DKD

**Table 4—Recommended dose adjustments for metformin based on eGFR**

| eGFR (mL/min/1.73 $m^2$) | Proposed action |
|---|---|
| ≥60 | No contraindication to metformin<br>Monitor kidney function annually |
| <60 and ≥45 | Continue use<br>Increase monitoring of renal function (every 3–6 months) |
| <45 and ≥30 | Prescribe metformin with caution<br>Use lower dose (e.g., 50%, or half-maximal dose)<br>Closely monitor renal function (every 3 months)<br>Do not start new patients on metformin |
| <30 | Stop metformin |

Adapted with permission from ADA (83).

# Sulphonylurea

| | |
|---|---|
| Class | Sulfonylureas (2nd generation) |
| Compound | ▪ Glibenclamide/Glyburide<br>▪ Glipizide<br>▪ Gliclazide<br>▪ Glimepiride |
| Mechanism | Closes $K_{ATP}$ channels on β-cell plasma membranes |
| Action(s) | ↑ Insulin secretion |
| Advantages | ▪ Generally well tolerated<br>▪ Reduction in cardiovascular events and mortality (UKPDS f/u) |
| Disadvantages | ▪ Relatively glucose-independent stimulation of insulin secretion: Hypoglycemia, including episodes necessitating hospital admission and causing death<br>▪ Weight gain<br>▪ May blunt myocardial ischemic preconditioning<br>▪ Low "durability" |
| Cost | Low |

ADA. V. Diabetes Care. *Diabetes Care* 2012;35(suppl 1):S22.
Adapted with permission from Silvio Inzucchi, Yale University.

**Gliclazide & glimepride** used in stage 3 with no dose adjustment..

**GLYBURIDE….NOT USED AT ALL**

| | | |
|---|---|---|
| TZDs | | |
| Pioglitazone | No dose adjustment required | 15–30 mg daily has been used (190) |
| α-Glucosidase inhibitors | | |
| Acarbose | Avoid if eGFR <30 mL/min/1.73 $m^2$ | Avoid use |
| Miglitol | Avoid if eGFR <25 mL/min/1.73 $m^2$ | Avoid use |
| GLP-1 receptor agonists | | |
| Exenatide | Not recommended with eGFR <30 mL/min/1.73 $m^2$ | Avoid use |
| Liraglutide | Not recommended with eGFR <60 mL/min/1.73 $m^2$ | Manufacturer does not recommend use (currently under study) |
| Albiglutide | No dose adjustment required | No clear guidelines exist—limited clinical experience in severe impairment of kidney function |

# Exenatide

- Exenatide is excreted by the kidneys.
- Exenatide clearance is ↓by 36% with a GFR of 45 mL/min/1.73m2 and by 64% with a GFR of 30 mL/min/1.73m2.
- Exenatide is not recommended with a GFR<30 mL/min/1.73 m2.
- Furthermore, exenatide has been associated with acute kidney injury or acceleration of CKD progression in case reports

# Liraglutide

- Liraglutide is fully degraded elsewhere in the body, and the kidneys are not a major organ of elimination.
- In single dosing, there is no adverse effects in subjects with stages 4 and 5 CKD.
- However, there are few data on long term use and the manufacturer recommends avoiding this medicine when GFR is < 60 mL/min/1.73 m2.

# DPP-4 Inhibitors

| DPP-4 inhibitors | | |
|---|---|---|
| Sitagliptin | 100 mg daily if eGFR >50 mL/min/1.73 $m^2$<br>50 mg daily if eGFR 30–50 mL/min/1.73 $m^2$<br>25 mg daily if eGFR <30 mL/min/1.73 $m^2$ | 25 mg daily |
| Saxagliptin | 5 mg daily if eGFR >50 mL/min/1.73 $m^2$<br>2.5 mg daily if eGFR ≤50 mL/min/1.73 $m^2$ | 2.5 mg daily |
| Linagliptin | No dose adjustment required | No dose adjustment required |
| Alogliptin | 25 mg daily if eGFR >60 mL/min/1.73 $m^2$<br>12.5 mg daily if eGFR 30–60 mL/min/1.73 $m^2$<br>6.25 mg daily if eGFR <30 mL/min/1.73 $m^2$ | 6.25 mg daily |

# KDOQI Diabetes Guideline 2012

## DPP-4 Inhibitors Dose Adjustment in Renal Impairment Patients

| DPP-4 Inhibitor | |
|---|---|
| **Sitagliptin** | GFR >50 ml/min/1.73 m² : 100 mg daily<br>GFR 30-50 ml/min/1.73 m² : 50 mg daily<br>GFR <30ml/min/1.73 m² : 25 mg daily |
| **Saxagliptin** | GFR >50 ml/min/1.73 m² : 5 mg daily<br>GFR ≤50ml/min/1.73 m² : 2.5 mg daily |
| **Linagliptin** | No dose adjustment |
| **Vildagliptin** | GFR ≥50 ml/min/1.73 m² : 50 mg twice daily<br>GFR <50 ml/min/1.73 m² : 50 mg once daily |

National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. *Am J Kidney Dis*. 2012;60(5):850-886.

National Kidney Foundation®
KDOQI

# SODIUM-GLUCOSE TRANSPORTER 2 INHIBITORS (SGLT2I)

## (GLIFLOZINS)

# SGLT2 I

- **Sodium-glucose co-transporter 2 (SGLT2)**
- **inhibitors work by blocking the reabsorption of filtered glucose in the kidneys.**

**.This leads to glucosuria and improved**

**glycemic control.**

# Effects of SGLT2 Inhibitors

**Inhibition of renal tubular $Na^+$-glucose cotransporter → reversal of hyperglycemia → reversal of "glucotoxicity"**

↑ Insulin sensitivity in muscle
- ↑ GLUT4 translocation
- ↑ Insulin signaling

↑ Insulin sensitivity in liver
- ↓ Glucose-6-phosphatase

↓ Gluconeogenesis
- ↓ Decreased Cori cycle
- ↓ PEP carboxykinase

↑ Improved beta cell function

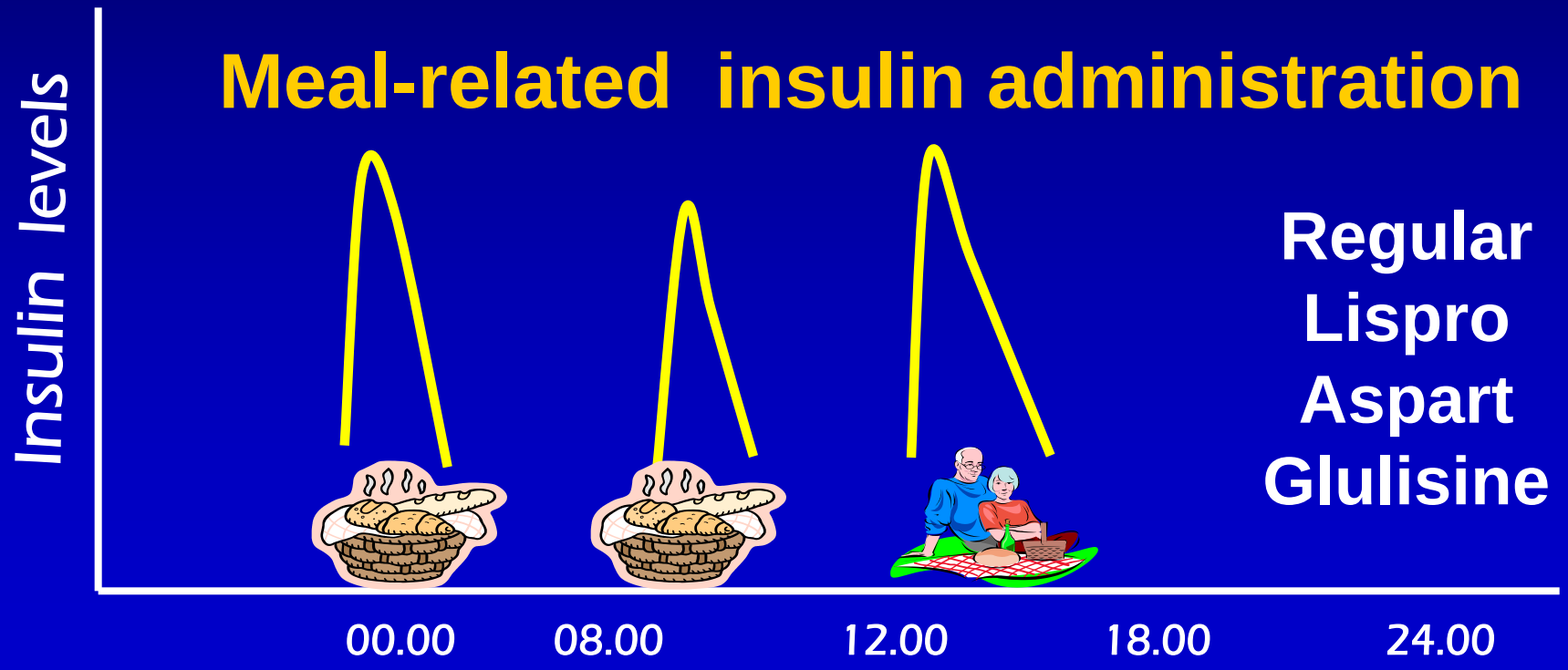
# SGLT2 Therapy: Contraindications and Caution

- Not effective among patients who have significant chronic kidney disease (eGFR < 45)
- Use with caution among patients sensitive to hypotension
  - Frail elderly patients
  - Patients with low SBP
  - Patients already on antihypertension medications
- Use with caution/warning among women with recurrent yeast infections

# Insulin

# Management Of Diabetes In CKD

## Insulin Regimen



# What's Next?

- Closed loops systems.
- Improved technology.
- Improved support systems.

# Use of conventional antidiabetic medications in T2DM with CKD

**Table 2** Use of conventional antidiabetic drugs in type 2 diabetic patients with chronic kidney disease

| | eGFR >60 mL/min | eGFR 30–59 mL/min | eGFR <30 mL/min | Dialysis |
|---|---|---|---|---|
| Insulin | ✓ | ✓ | ✓ dose reduction | ✓ dose reduction |
| Metformin | ✓ | ✓ caution | ⊘ | ⊘ |
| Sulfonylureas | ✓ | caution | caution | ⊘ |
| Metiglinides | ✓ | ✓ caution | caution | ⊘ |
| Thiazolidinediones | ✓ | ✓ caution | ✓ caution | ✓ caution |
| Alpha-glucosidase inhibitors | ✓ | ✓ | ⊘ | ⊘ |

**Note:** ⊘, use not allowed.

**Abbreviation:** eGFR, estimated glomerular filtration rate.

# Improved Glycemic Control Has Been Shown to Reduce the Risk of Complications

According to the United Kingdom Prospective Diabetes Study (UKPDS) 35, Every 1% Decrease in A1C Resulted in:

21%

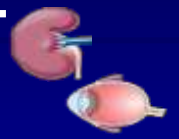
Decrease in risk of any diabetes-related end point (*P*<.0001)

14%

Decrease in risk of MI (*P*<.0001)

12%

Decrease in risk of stroke (*P*=.04)



37%

Decrease in risk of microvascular complications (*P*<.0001)

Stratton IM et al. *BMJ.* 2000;321:405-412.

# Be Positive…..always..!!!!!!!

# Treatment of End-Stage Renal Disease (ESRD)

Hemodialysis

Peritoneal Dialysis

Renal Transplantation

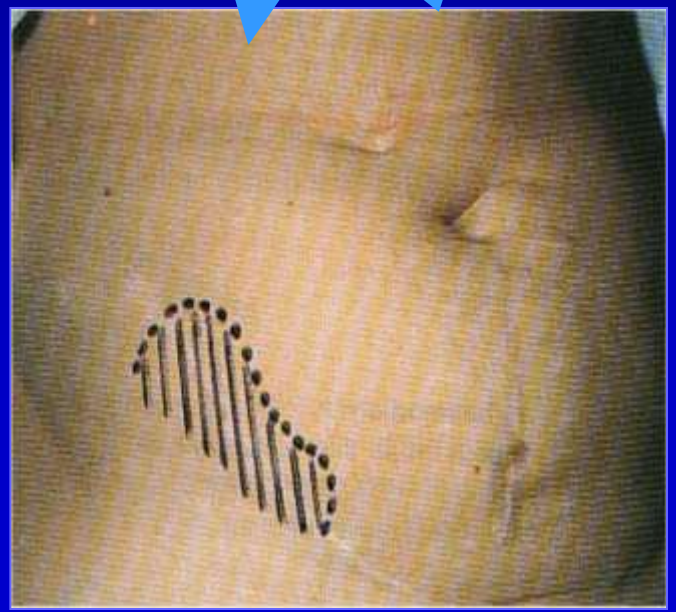


**Table 4. Summary of Recommendations for Care of Patients With Diabetes and CKD**

| Management Issue | | Outcome/Action |
|---|---|---|
| Diagnosis | | Urinalysis for protein<br>Serum creatinine – eGFR |
| Measurement of glycemic control | | A1C<br>Blood glucose meter |
| Medications | Insulin | May need to decrease dose |
| | Oral hyperglycemic agents | May need to decrease dose or discontinue use |
| Comorbid diseases | Blood pressure | ACE inhibitors/ARBs |
| | Hyperlipidemia | May need to decrease dose |
| Complications of CKD | | Anemia, hyperphosphatemia, hyperparathyroidism |
| Nutrition | | Avoid high protein intake; reduce sodium intake; reduce potassium intake; reduce phosphorus intake |

# Conclusions

- DM is a huge & complex disease with multiple etiologies.
- Diabetes is the leading cause to multiple organ-system complications espcially CKD & ESRD.
- Glycemic control is important to reduce the risk of DM complications.
- Hypoglycemia, progression of renal dysfunctions & staging CKD are the main challenges during diabetes management.
- Manage carefuly dyslipidemia & HTN in DCD.
- Oral hypoglycemic agents can be used (not all) with dosage correction and adjustment.
- Insulin is still a cornerstone in management of DKD.


DOCTOR
TEAM
PATIENT

# DCDC I7th,20-22 April,2016, Ras Elbarr,Domyat

# Thank You